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09/724,872	11/28/2000	Gyula Hadlaczky	24601-402F	8394

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HELLER EHRMAN WHITE & MCAULIFFE LLP
4350 LA JOLLA VILLAGE DRIVE
7TH FLOOR
SAN DIEGO, CA 92122-1246

EXAMINER
HELMER, GEORGIA L

ART UNIT	PAPER NUMBER
1638	17

DATE MAILED: 11/07/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/724,872	Applicant(s) HADLACZKY ET AL.	
	Examiner Georgia L. Helmer	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) *2,3,5,8-10,13-15,17-19,21-28 and 31-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1,4,6,7,11,12,16,20,29 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4, 7, 10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *IDS No 13 and 16*. .

DETAILED ACTION

Restriction election

1. The Office acknowledges the receipt of Applicant's restriction election, Paper No. 15, filed 8 August 2002. Applicant elects Group I claims 4, 6, 7, 16, 20, 29, and 30, as drawn to plants cells and plant SATACs, with traverse. Claims 2-3, 5, 8-10, 13-15, 17-19, 21-28 and 31-33 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 15, filed August 2, 2002.

Applicant's traversal is on several ground(s). The first ground is that there would be no search burden by virtue of the fact that this application is a continuation-in-part (CIP) of two patents claiming satellite artificial chromosomes (SATACs). As a result, Applicant asserts that SATACs are presumptively novel, unobvious and enabled. Applicant's second ground of traverse asserts that the restriction possesses the possibility of never getting a generic claim examined. Applicant's third ground asserts that there is nothing of record that establishes that introduction of a plant SATAC into an animal cell or introduction of an animal SATAC into a plant cell are distinct processes, nor that plant and animal SATACs function differently. In this regard, Applicant offers a declaration to demonstrate that the same methods can be used to introduce either plant or animal SATACs into either plant or animal cells. Applicant also asserts that the burden is on the Office to support statements made in the restriction requirement, referring specifically to MPEP 2144.03. These arguments fail to persuade. The first

two grounds of traversal were first set forth in the record in Applicant's earlier response of Paper No. 11, filed May 16, 2002. Both of these earlier grounds of traversal were adequately addressed in the modified restriction requirement of Paper No. 14, mailed July 16, 2002. Accordingly, no further discussion of the first two grounds of traversal is necessary herein. With regard to Applicant's third ground of traverse, the Office initially notes that MPEP 2144.03 is not directed to assertions made in support of restriction requirements as herein, but is instead directed to positions taken by the Office with regard to patentability determinations, and more particularly, to rationale supporting an obviousness rejection. This is simply not the case here and therefore, MPEP 2144.03 is generally not applicable to the current situation. Turning instead to the merits of Applicant's argument that the same methods can be used to introduce either plant or animal SATACs into either plant or animal cells, the Office notes that Applicant has not clearly and unequivocally conceded that plant SATACs are unpatentable over animal SATACs or that their use in plant cells is unpatentable over their use in animal cells. Instead, Applicant asserts that the same methods work for both systems. By methods, the Office notes that Applicant must mean the same methodology, since the material being used is not the same (animal SATACs and cells versus plant SATACs and cells). Two methods may be patentable, one over the other where the material being used is different or where the population of cells being treated is different, even where the manipulative steps are the same. Such appears to be the situation here. Accordingly, absent a clear and unequivocal statement by Applicant that the methods as between use of plant and animal SATACs and cells are not separately patentable, the restriction

there between is maintained for reasons of record. Applicant should note that if such a statement is provided, the restriction would be modified accordingly, though any reference usable against a plant SATAC or cell would be likewise useable against an animal SATAC or cell.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-33 are pending. Claims 2-3, 5, 8-10, 13-15, 17-19, 21-28, and 31-33 are nonelected. Claims 1, 4, 6, 7, 11, 12, 16, 20, 29, and 30 are examined in the instant application.

3. Claims 16 and 20 are objected to because the nonelected invention should be deleted from the claims.

Information Disclosure Statement

4. Initialed and dated copies of Applicant's IDS form 1449, Paper No. 4 (5/29/01), 7 (9/18/01), 10 (4/9/02), 13 (6/3/02), and 16 (8/28/02) are attached to the instant Office action.

Claim Rejections - 35 USC § 112, second paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 11, 12, 16 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 11, it is unclear how the final step of "selecting a cell" relates to "introducing a DNA fragment" and ""growing the cell" in the overall flow of the method steps.

Clarification and/or correction are required.

Claim Rejections - 35 USC § 112.1 Enablement

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1, 4, 6, 7, 11, 12, 16, 20, 29 and 30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a mammalian SATAC in a mammalian cell, does not reasonably provide enablement for any SATAC in any cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant's invention relates to methods for preparing cell lines containing artificial chromosomes, methods of isolating artificial chromosomes and methods for delivery of artificial chromosomes to selected cells and tissues.

Applicant discloses an animal SATAC. Applicant's claims are drawn to any SATAC. Mammals, and animals, are not representative of plants in terms of chromosomes and chromatin structure. In animals and in yeast, satellite DNA is AT-rich, whereas plant satellite DNA tends to be GC-rich (Ferl, R et al in Buchanin, et al. Biochemistry & Molecular Biology of Plants (2000) American Society of Plant Physiologists, Rockville Md 20855, page 324.) GC-rich DNA differs in physical properties from AT-rich DNA; GC rich DNA is more compact and dense, reflecting its more highly hydrogen-bonded structure (Lehninger, A. Biochemistry. 2nd edition, 1976, Worth Publishers, New York. p 864). It is unclear how compact, densely H-bonded DNA affects SATAC activity and function. Furthermore, telomeres, origin of DNA replication and a centromere are required for function of a SATAC (Willard, HF, Science, 290, pps 1308-9, 2000). It is unclear what telomeres, origin of DNA replication and centromere are necessary for other than animal SATACs, whether additional components are required, or how to isolate or construct functional SATAC in all cells, or non-mammalian cells. Plant centromeres have yet to be physically constructed or isolated. However, plant centromeres of Arabidopsis have been defined by genetic and sequence analysis (Copenhaver, et al, Science, 286, December, 1999, pages 2468-2474). Centromeres of artificial chromosomes appear to show some species-specific behavior in animal systems (Willard, HF, Science, 290, pps 1308-9,

2000; Shen, et al, Current Biology 10, 31-34, 2000; Telenius, et al, Chromosome Research 7, pages 3-7, 1999; Ferl, R et al in Buchanan, et al. Biochemistry & Molecular Biology of Plants (2000) American Society of Plant Physiologists, Rockville Md 20855, page 324,5). It is unpredictable that plants, from a totally different Kingdom than animals, would have centromeres which are structurally and biochemically the same as those of animals. Neither the Applicant, nor the prior art, teach how to isolate or make plant centromeres, nor how to make a SATAC having a plant centromere. Rather it is predictable that plant centromeres would differ from animal centromeres, since animal centromeres differ among themselves and show species-specific behavior. Patterns of heterochromatin differ between animal and plants, with animals showing heterochromatization in telomeres, centromeric, and pericentrometic regions. In plants, however, heterochromatin is located at the nucleolar organizer, and at the chromosome knobs. See Avramova, Plant Physiology, 2002, vol 129, pages 40-49. Plant heterochromatin differs from animal heterochromatin in the absence of proteins similar to known heterochromatin proteins, location of potentially active genes in the knob structures and in the periocentromeric regions of plant genome, and different chromosomal environments for collinear genes in related species (Avramova, op cit, p 41). In fact plants have a family of 20 methyltransferase enzymes unique to plants, putatively representing host factors necessary for proper function of plant systems and not required in other systems. Therefore, given that plant satellite DNA, plant centromeres and plant heterochromatin differ from their animal counterparts, it is

unpredictable that a plant SATAC, consisting of those components, would function as desired in the claimed invention.

Simple heterologous expression constructs in animal host systems are clearly structurally different from heterologous expression constructs in other host systems, including plants. Required are different promoters, enhancers, codon optimization, termination regions, and other regulatory regions. One of skill in the art would expect a SATAC constructed for mammalian cells to differ from a SATAC functional in a non-mammalian cell. SATACs are much more complex, than just the mere heterologous expression system, and require manipulation of much larger size DNA. The transfer of large pieces of DNA between cells in a major problem in artificial chromosome technology (Brown, Trends in Biotech, 2000, vol 18, p 403; Perez, et al, Trends in Biotech, 2000, 18, 402-3; Willard, HF, Science, 290, 1308-9, 2000; Hadlaczky, Curr. Opin. Mol Ther, 2001, vol 3, pages 125-32, p 129).

It is unclear what regions of Applicant's animal SATAC should be retained, and what regions should be modified, to obtain a SATAC that would be operable in a non-mammalian cell. The art of artificial chromosome technology is in its infancy (Willard, HF, Science, 290, pps 1308-9, 2000, final paragraph). Therefore, much greater guidance would be required. Applicant teaches an animal SATAC in a mammalian cell. Applicant does not address any of the issues set forth above. While one skilled in the art can readily make necessary changes to Applicant's mammalian SATAC to generate a non-mammalian SATAC, guidance is required as to what those changes are. To require one skilled in the art to randomly make changes to Applicant's animal SATAC,

or to generate their own SATAC constructs without guidance as to how inoperable embodiments can be readily eliminated other than by trial and error, is an invitation to experiment, requiring excessive and undue experimentation. Accordingly Applicant has not sufficiently enabled a SATAC generated from any source as commensurate in scope with the claims.

Applicant discloses human, mouse, and hamster cells. The claims are drawn to any cell, including, any non-mammalian animal, any plant, any yeast and any bacteria. While mammalian and nonmammalian cells have been extensively used to express heterologous constructs, the constructs much be recognized by the cell machinery. Otherwise, the construct would be degraded or removed from the cell. No construct to date is universally recognized in all cells. One skilled in the art would expect that a SATAC construct for a mammalian cell would also differ from a SATAC construct for a bacteria cell, a yeast, cell, a insect cell, and a plant cell.

Applicant does not disclose that the SATAC of the instant application is universally adapted to be operable in all cell types. Applicant has only shown that Applicant's SATAC is operable in a mammalian cell. It is unpredictable that Applicant's SATAC would be operable in all cell types. Accordingly, Applicant has only enables Applicant's SATAC for a mammalian cell. Thus Applicant is not enabled for using an SATAC in any cell type, as commensurate in scope with the claims.

Remarks

9. No claim is allowed.

10. The claims are free of the prior art.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Georgia L. Helmer whose telephone number is 703-308-7023. The examiner can normally be reached on 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 703-306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Georgia Helmer, PhD
Patent Examiner,
Art Unit 1638
October 30, 2002

Phuong Bui
PHUONG T BUI
PRIMARY EXAMINER
10/30/02